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October 15, 1992

Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

RECEIVED
8/24/95

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

- othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

CAS# 7440-03-1; 10026-12-7; 1313-96-8; 1314-62-1; 7721-01-9
 # for niobium oxychloride not known
CHEM: Niobium metal; Niobium pentachloride; Niobium oxychloride, Niobium pentoxide; Tantalum pentachloride; Vanadium pentoxide
TITLE: Toxicity of Compounds of Niobium, Tantalum, and Vanadium
DATE: 12/9/57
SUMMARY OF EFFECTS: Gastric injury with Niobrium pentachloride; Tantalum pentachloride.

TOXICITY OF COMPOUNDS OF NIOBIUM, TANTALUM, AND VANADIUM

Medical Research Project No. MR-166

In order to anticipate possible danger from human exposure to chemicals concerned with preparation of niobium metal from columbite ore, the Pigments Department (1 and 2) requested an investigation of the toxicity of the following compounds:

(1) Niobium Metal - (Haskell No. 1887)
(2) Niobium Pentachloride - (Haskell No. 1886)
(3) Niobium Oxychloride - (Haskell No. 1885)
(4) Niobium Pentoxide - (Haskell No. 1943)
(5) Tantalum Pentachloride - (Haskell No. 1888)
(6) Vanadium Pentoxide - (Haskell No. 1942)

The Haskell Laboratory has determined the acute oral toxicity of samples 1, 2, 3, and 5 using the rat as the test animal.

In order to predict the effects on the lung of inhalation of dust of samples 1, 3, 4, and 6, the dust was introduced into the peritoneal cavity of guinea pigs. Half of the animals were sacrificed thirty days, and the remainder sixty days, after dosing. Experience with this test has shown that the reaction of the peritoneal tissue to the dust is similar to that of lung tissue to inhaled dust.

NIOBIUM METAL

Acute Oral Toxicity

Due to the small amount of sample available, a single dose of 7500 mg/kg of the metal in a finely granular form was administered to a 330 gm white male rat by stomach tube as a 30 per cent suspension in 2 per cent aqueous gum guar. It caused no detectable clinical signs of toxicity. During the first twenty-four hours, 62.5 per cent of the niobium metal was recovered from the feces. No pathological change attributable to the niobium was found when the rat was sacrificed ten days after treatment.

Tissue Reaction

About 0.5 gm niobium metal in a No. 5 gelatin capsule was introduced under light pentobarbital anesthesia into the peritoneal cavity of each of ten guinea pigs weighing 410 to 450 gm. No attempt was made to sterilize the metal or the capsule, but the surgical operation was carried out with aseptic precautions. The animals lost weight during the first week after operation and then gained weight and behaved normally until sacrificed after one and two months. The

cross-indexed under each of the above underlined compounds

niobium metal was found, at autopsy, in one or more masses loosely attached to the peritoneal surfaces, often hanging in the form of a black globule from the omentum. Elsewhere the surfaces of the abdominal organs were smooth and normal in appearance and without adhesions or other evidence of irritation, except as caused by the operation. The organs themselves appeared normal. Microscopically, the particles of material had the same appearance as before injection. They were found as masses on the peritoneal surfaces or were held together by mononuclear cells and a very few connective tissue cells. There was no microscopic evidence of any inflammatory type of reaction and no evidence that the particles had penetrated the peritoneal surfaces. Comparison of the lesions after one and two months showed no difference.

NIOBIUM PENTACHLORIDE

Acute Oral Toxicity

Fifteen per cent and 30 per cent solutions were made in dehydrated peanut oil. Reaction occurred on the surface, presumably due to atmospheric moisture with the formation of hydrochloric acid and niobium oxychloride. The pH of the solution was approximately 1 as determined by indicator paper. When doses ranging from 450 mg/kg to 7500 mg/kg were administered to adult male albino rats by stomach tube, the Approximate Lethal Dose (ALD) was established at 3400 mg/kg. The lethal doses produced pallor, labored breathing, and great discomfort with death within three hours. Sublethal doses as low as 670 mg/kg caused pallor and discomfort with occasional weight losses. At autopsy all animals, including survivors sacrificed ten or eleven days after treatment, showed evidence of gastric injury.

NIOBIUM OXYCHLORIDE

Acute Oral Toxicity

The ALD of niobium oxychloride as a 30 per cent suspension in peanut oil, administered by stomach tube to rats, was greater than 11,000 mg/kg - the largest practical dose. No pathological change due to the treatment was found when the animals were sacrificed nine days after treatment.

Tissue Reaction

A 5 per cent aqueous suspension of the sample was sterilized at 15 pounds of steam pressure for 15 minutes and injected in 2 ml quantities intraperitoneally into each of ten young guinea pigs weighing 350 to 440 gm. The animals continued a normal weight gain and behavior without initial setback after injection, with the exception of one which developed extensive pneumonia and peritonitis after about

one month and was sacrificed when moribund on the 32nd day. The remaining animals sacrificed thirty and sixty days after treatment showed the injected material accumulated in several white masses on the peritoneal surfaces, principally on the most dependent ventral peritoneal wall. Elsewhere there was no evidence of abnormality. Microscopically the tissue reaction was like that to niobium metal, but slightly more pronounced. The accumulated particles were held together by monocytes, a few giant cells and a small amount of connective tissue and blood vessels. There was no evidence of a continuous type of inflammatory reaction, and no evidence of penetration of the peritoneum. Comparison of the lesions after thirty days with those after sixty days showed very little, if any, change - a response which is typical for inert dusts such as titanium dioxide.

NIOBIUM PENTOXIDE

Tissue Reaction

A sterilized 5 per cent aqueous suspension, injected in 2 ml quantities into the peritoneal cavities of each of ten guinea pigs weighing 335 to 390 gm, was followed by no detectable clinical evidence of injury due to the chemical. One animal died of lobar pneumonia seven days after injection. The injected material was found massed on the most dependent part of the peritoneal cavity where it was covered with a single layer of thin cells. The material was so densely packed that cellular detail within the mass could not be made out. However, there was no acute inflammatory reaction and none of the material had entered the underlying muscle.

A second animal, dead of lobar pneumonia thirteen days after injection, showed a similar accumulation of the injected material on the peritoneal surface without any evidence of acute inflammatory reaction.

The remaining eight guinea pigs remained healthy and gained weight normally until sacrificed thirty-one and sixty days after injection. In all animals the material was found in masses on the peritoneal surfaces, mostly on the most dependent ventral surface. The tissue reaction was the same as to niobium oxychloride. Individual particles were densely accumulated within monocytes and a few giant cells which, in turn, were densely packed in smooth, slightly raised, white masses up to about 1 cm in diameter. A few connective tissue cells and blood vessels held the accumulations together. Comparison of thirty-one-and sixty-day-lesions showed the tissue reaction to be essentially static, without evidence of continuous inflammatory reaction. None of the material was found penetrating the underlying tissue.

TANTALUM PENTACHLORIDE

Acute Oral Toxicity

Preparation of 15 per cent and 30 per cent solutions in dehydrated peanut oil formed a dark brown liquid and white precipitate, presumably due to reaction with atmospheric water at the surface with the formation of tantalum oxide and hydrochloric acid. The final pH was approximately 1 as determined by indicator paper. Doses ranging from 450 mg/kg to 7500 mg/kg administered by stomach tube to adult male albino rats established the ALD at 1500 mg/kg. One rat receiving 3400 mg/kg survived. The lethal doses produced pallor, great discomfort, and death within eighteen hours. A dose of 1000 mg/kg caused pallor and discomfort but lower doses were apparently tolerated. However, anatomical evidence of gastric injury was found in all animals ten or fourteen days after treatment. At 670 mg/kg there was a penetrating ulcer of the stomach.

VANADIUM PENTOXIDE

The material as received was a brown powder consisting of rhomboid crystals averaging 36 microns in length and accumulated in masses as large as 125 microns in diameter. The immediate pH of a 5 per cent aqueous suspension was 6 as determined by indicator paper, and after sterilization at 15 pounds pressure for 15 minutes the pH was 2.

Tissue Reaction

Two ml of a 5 per cent aqueous sterilized suspension, injected intraperitoneally into ten guinea pigs weighing 340 to 405 gm, was followed by rapidly progressing diarrhea and death of all but one animal in one or two days. To minimize the acidity of the material injected, the experiment was repeated with five guinea pigs using vanadium pentoxide and water sterilized separately and mixed just before use. The dose given some of the animals was reduced one-half. The results were the same, only one animal surviving thirty-six hours.

Examination of the animals dying within two days was unsatisfactory because of post-mortem change. The injected material was massed on the peritoneal surfaces. No gross evidence of inflammatory reaction was detected. One guinea pig lived one week after injection of 50 mg of vanadium pentoxide (1 ml of a 5% suspension), during which it suffered from diarrhea and weight loss. The injected material was found accumulated on the peritoneal surface accompanied by an inflammatory reaction which might have been due to bacterial contamination.

One of the thirteen guinea pigs injected with 100 mg of vanadium pentoxide (2 ml of a 5% suspension) survived but remained in poor condition for two weeks. It then rapidly regained weight and the general appearance of good health. When it was sacrificed thirty-two days after injection, no evidence of the vanadium pentoxide was found, and no pathological change was recognized.

DISCUSSION

The injury following oral administration of niobium pentachloride and tantalum pentachloride was presumably due to the heat and hydrochloric acid evolved by the reaction with the water contained in the stomach and within the tissue of the stomach wall. The lesions were severe and might lead to chronic ulcer or penetration.

Although niobium metal, niobium oxychloride, and niobium pentoxide were found to be innocuous when given by mouth or injected intraperitoneally, inhalation in the form of dusts might result in residual deposit in the lungs, depending on th[illegible] size

The tissue reaction to niobium metal was practically nil. The particles were collected and massed by cells especially performing this function. Thereafter, the adjacent tissues simply accommodated themselves to the mass. The reaction was the same as the physical accommodation with minimal biological reaction in the use of tantalum as suture material, prosthetic devices, and thin sheets applied to burned surfaces (3).

" The tissue reaction to intraperitoneal injection of niobium oxychloride and niobium pentoxide, although inert in type, involved more connective tissue and blood vessel reaction than niobium metal, but not more than would result from such a dust as titanium dioxide (7). From the point of view of inhalation hazard, it should be pointed out that atmospheric contamination resulting from the escape of niobium pentachloride or tantalum pentachloride would produce the oxychlorides or oxides of small particle size accompanied by hydrochloric acid. The simultaneous inhalation of the two could cause greater tissue reaction than indicated by the results reported here. "

The results with vanadium pentoxide are in accord with those of Sjoberg (4) who found that an intraperitoneal injection of 34-45 mg was fatal to guinea pigs, and some deaths followed the injection of 5-10 mg. There was no evidence of peritoneal reaction in the animals dying within five days and survivors recovered completely in three to ten weeks.

It is probable that vanadium pentoxide is soluble in body fluids since Talvite and Wagner (5) recovered 61 per cent of sodium vanadate from the urine and feces of rats twenty-four hours

after intraperitoneal injection of the oxide. After two weeks, 11 per cent of the injected material was found retained in the tissues.

There is general agreement that the inhalation of vanadium pentoxide by man and animals causes irritation of the respiratory tract and sometimes of the digestive tract as well (6). The toxic action is believed by some workers, cited by Sjoberg (4), to be in the nature of damage to the metabolic processes in the tissues, although this has not been proved. Flury and Zernick, also cited by Sjoberg, proposed that the poisoning is due to a catalytic action on the tissues in the respiratory and digestive organs and in the nervous system. The Maximum Acceptable Concentration (MAC) for V_2O_5 dust in the atmosphere is 0.5 mg/m^3.

CONCLUSIONS

Niobium metal, niobium oxychloride, and niobium pentoxide are substances of low toxicity and there should be no danger from short periods of inhalation of the dust in moderate amounts. However, the MAC in the atmosphere should not exc[illegible] for particles of 1 to 5 microns in diameter, the value established for nuisance dusts.

Contact with niobium pentachloride and tantalum pentachloride may be harmful because of the heat and hydrochloric acid evolved in the presence of moisture.

Vanadium pentoxide causes a tissue reaction entirely different in type from that caused by such insoluble and almost insoluble materials as the oxides of titanium, niobium, tantalum on the one hand, and silicon on the other hand. It has a fairly marked toxic effect when introduced intraperitoneally into guinea pigs. The substance appears to be absorbed and carried away, causing a systemic toxic reaction and leaving no sign of anatomical injury. Although vanadium pentoxide in the guinea pig peritoneal cavity does not cause fibrosis, inhalation of the dust is known to cause irritation of the respiratory tract. Both inhalation and ingestion of vanadium pentoxide should be avoided.

REFERENCES

(1) Letter: W. G. Bowles to J. A. Zapp, February 25, 1957.

* Millions of particles per cubic foot of air.

(2) Letter: C. G. Moore to J. A. Zapp, July 10, 1957.

(3) Olson, C. T., Industrial Medicine and Surgery, 13:917, 1944.

(4) Sjoberg, S., Acta Med. Scandinav., 138, Supplement 238, 1950.

(5) Talvite, N. A. and Wagner, W. D., Arch. Ind. Hyg., 9:414, 1954.

(6) McTurk, L. C., et al, Industrial Medicine and Surgery, 25:29, January, 1956.

(7) Haskell Laboratory Medical Research Report MR-199, "Toxicity of Titanium Tetrachloride - Further Studies", December 5, 1949.

HASKELL LABORATORY FOR TOXICOLOGY
AND INDUSTRIAL MEDICINE

Report by: Douglas M. Gay
Douglas M. Gay, M.D.
Pathologist

Approved by: John A. Zapp, Jr.
John A. Zapp, Jr.
Director

DMG/ah
12-5-57
Report No. 49-57

TOXICITY OF COMPOUNDS OF NIOBIUM, TANTALUM, AND VANADIUM

Medical Research Project No. MP-166

Report No. 49-57

Approved for toxicology:

D. B. Hood
Chief, Toxicology Section

12-9-57

Triage of 8(e) Submissions

Date sent to triage:_____ NON-CAP (CAP)

Submission number: 12413A TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Gordon Cash (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN w/NEUR

Group 3 -HERD (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.):_____

Notes:

☒ This is the **original** 8(e) submission; refile after triage evaluation.

☐ This **original** submission has been **split**; rejoin after triage evaluation.

☐ Other:

Photocopies Needed for Triage Evaluation

entire document: (0) 1 2 3

front section and CECATS: (0) 1 2 3

Initials: JCS **Date:** 6/26/96

Please finish evaluating. Vanadium pentoxide and Niobium pentoxide were not looked at.

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 1092 - 12413 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 08/24/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0670) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER BENEFITS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:

CAS#
7440-03-1
10026-12-7
1313-96-8
1314-62-1
7721-01-9
Niobium oxychloride unknown

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY
(YES)
(CAS SR)
NO
IN TRANSIT

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT
GP

TOXICOLOGICAL CONCERN:
(LOW) Acute Oral Toxicity, Acute IP Toxicity
MED
HIGH

USE:

PRODUCTION:

COMMENTS

12413A

1 Niobium Metal

L

Acute oral toxicity is of low concern based on the survival of one rat exposed to 7500 mg/kg. No clinical signs or pathological changes were observed. [Acute intraperitoneal resulted in no toxicity in 10 guinea pigs exposed to 0.5 g.]

2 Niobium Pentachloride

L

Acute oral toxicity is of low concern based on an approximate lethal dose of 3400 mg/kg in rats exposed to doses ranging from 450-7500 mg/kg. Clinical signs included pallor and discomfort (lethal doses, sublethal ≥670), and labored breathing (lethal doses). All animals exhibited gastric injury.

3 Niobium Oxychloride

L

Acute oral toxicity is of low concern based on an approximate lethal dose of >11000 mg/kg in rats. [Acute intraperitoneal exposure resulted in no toxicity in 9/10 guinea pigs exposed to a 5% aqueous suspension. One guinea pig developed extensive pneumonia and peritonitis.]

4 Tantalum Pentachloride

L

Acute oral toxicity is of low concern based on an approximate lethal dose of 1500 mg/kg in rats exposed to doses ranging from 450-7500 mg/kg. Gastric injury was observed in all animals, and a penetrating ulcer at 670 mg/kg. Clinical signs included pallor and discomfort at lethal doses and at 1000 mg/kg.

VANADIUM PENTOXIDE

7721-01-9

"12413A-02"="1X"="ABSTRACT BASED ON SUMMARIZED RESULTS SUBMITTED WITHOUT A REPORT. A 2 ML 5% SOLUTION OF VANADIUM PENTOXIDE (CAS# 7721-01-9) WAS INJECTED INTO PERITONEAL CAVITIES OF 10 GUINEA PIGS. RAPIDLY PROGRESSIVE DIARRHEA, FOLLOWED BY DEATH IN 9/10 ANIMALS, OCCURRED 1-2 DAYS POST-DOSING. INJECTED MATERIAL WAS FOUND MASSED ON PERITONEAL SURFACES WITH NO EVIDENCE OF INFLAMMATORY REACTION.

EXPERIMENT WAS REPEATED AT HALF-DOSE WITH 5 GUINEA PIGS. ONLY 1/5 ANIMALS SURVIVED 36 HOURS."

NIOBIUM PENTOXIDE

1313-62-1

"12413A-01"="N"="ABSTRACT BASED ON SUMMARIZED RESULTS SUBMITTED WITHOUT A REPORT. A 2 ML 5% SOLUTION OF NIOBIUM PENTOXIDE (CAS# 1313-62-1) WAS INJECTED INTO PERITONEAL CAVITIES OF 10 GUINEA PIGS. TWO ANIMALS DIED OF LOBAR PNEUMONIA 7 AND 13 DAYS AFTER INJECTION. TEST MATERIAL WAS MASSED IN THE PERITONEAL CAVITY WITH NO ACUTE INFLAMMATORY REACTION NOTED. THE REMAINING 8 ANIMALS WERE SACRIFICED 31 AND 60 DAYS AFTER INJECTION. TEST MATERIAL WAS FOUND MASSED WITHIN MONOCYTES ON THE PERITONEAL SURFACES. NO SIGNS OF TOXICITY WERE NOTED."